

P R A C E O R Y G I N A L N E

CERVICAL INTRAEPITHELIAL NEOPLASIA - BIOPSY METHODS AS AIDS FOR DIAGNOSIS AND THERAPY

J. QUAAS, M. BUDNER, J. HEINRICH

W 1999 r., w Niemczech konizacja jest preferowaną metodą diagnostyczną w przypadkach wewnątrz nabłonkowej szyjkowej neoplazji (CIN). Morfolodzy uważają konizację za najlepszą metodę dla histologicznej weryfikacji CIN, ponieważ uzyskany materiał pozwala na topograficzne usytuowanie obserwowanych patologicznych zmian nabłonkowych. Jednakże ze względu na fakt, że obserwuje się z jednej strony stały, przeciętny spadek wieku pacjentek z CIN, a z drugiej strony średni wiek pierworódek wzrasta konizacja jako pierwsza, diagnostyczna procedura może nie być szeroko akceptowana przez klinicystów. Od chwili pojawienia się nowych technik operacyjnych jak konizacja laserowa lub elektrochirurgiczna zabieg jest wykonywany ambulatoryjnie, a ryzyko powikłań uległo znacznemu obniżeniu. U 5% leczonych wymagana jest dodatkowa terapia związana z krwawieniem, liczba pozostałych komplikacji pozostaje stała, podczas gdy późnych powikłań w wielu przypadkach nie można łączyć z zabiegiem. Odnosi się to do organicznej możliwości wykonania następowych badań kolposkopowych i cytologicznych, zwężenia kanału szyjki macicy z następową haematometrią albo dystocją szyjki macicy w czasie porodu, endometriozą szyjki macicy, poronieniami lub porodami przedwczesnymi.

According to the conventional procedure, indication of conisation is almost exclusively based on cytologic findings. The large number of false-positive histological findings is disregarded. Verification examinations are only recommended for the cytologic finding of Pap III, whereas a one-time Pap IVa is considered to be sufficient as indication. Numerous authors caution about as many as 30% of false-negative and false-positive cytologic results (7, 12, 14, 17). If the cytologic test is the only basis for indication, correspondence between preoperative cytology and postoperative histology is low.

Since it is indispensable to check suspect cytologic findings by means of histological examinations, clinicians should opt for simple, but adequately safe biopsy. When it comes to selecting a suitable biopsy procedure for suspect or pathological cytologic tests, the potential of colposcopic techniques is often underestimated.

In the US and numerous West European countries, biopsy combined with cervical abrasion is preferred to conisation.

As early as 1979, (Egger et al) (3) discussed the advantage of obtaining histological clarification of the state of the uterine cervix by performing only ectocervical surface

scraping and cervical abrasion. The advantages of this simple procedure over conisation and vaginal hysterectomy have been demonstrated statistically for more than 1000 interventions performed over a period of 15 years, and they have been recommended for medical practice.

Against this background we have conducted a retrospective analysis of various biopsy techniques, such as single and multiple biopsy of the ectocervix, scraping of the entire surface epithelium of the ectocervix and cervical abrasion.

MATERIAL AND METHOD

All cases hospitalised for cytologic findings of groups Pap III, IIID, IVa and IVb during the period between 1977 and 1995 were evaluated. In a total of 1610 patients 1182 conisations with cervical abrasion (CA) and 428 ectocervical surface scrapings with cervical abrasion (ESS/CA) were performed. In 130 cases, histological evidence of colposcope-guided biopsy (PE) was additionally compared with the findings of subsequent ectocervical surface scrapings. The distribution of histological findings is shown in the charts. Smears were assessed by numerous laboratories in accordance with the SOOST classification. Morphological examination of all tissue samples was carried out at the Pathological Institute of the Klinikum Stralsund.

Starting in 1985, combined biopsy techniques as well as conisation were always followed by CO₂-laser vaporisation at max. 20 W. Aided by a colposcope, circular vaporisation of the entire ectocervix and the atypical regions was performed; they were divided in four sectors and systematically destroyed. Being performed after the ectocervical surface scraping, the objective of this technique was to obliterate the epithelium with its crypts up to a depth of 9 mm. The intention was to combine, as in conisation, clarification based on biopsy and definitive therapy. As a rule, conisation was performed within 6 weeks in all patients with CIN III findings.

RESULTS

Of 1610 patients who were hospitalised for pathological cytologic findings of Pap III, IIID, IVa or IVb from 1977 to 1995, 35.2% had findings of (CIN I. At 23.2 %, the rate for the 1182 conisations alone was clearly too high. Even if histological findings indicating only abnormal epithelium and CIN I were used as less stringent selection criteria, the percentage was still unsatisfactory, i.e. 13.9% (Fig. 1). When we subdivided the entire period into one phase preceding the introduction of a second biopsy technique (1977-1984, n = 468) and one following it (ectocervical surface scraping, 1985-1995, n = 714), the resultant numbers for findings of (CIN I were 17.7 % and 11.3%, respectively (Fig. 2).

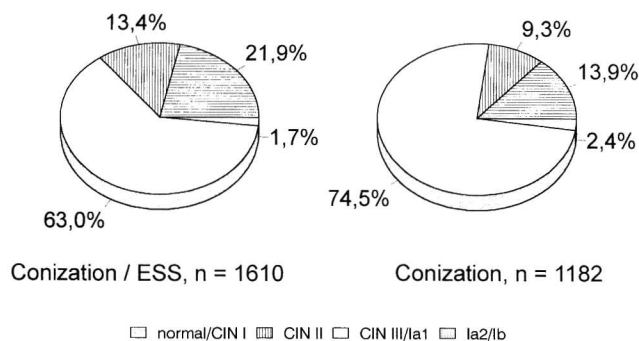


Figure 1. Pap III/IV and histological findings post conisation or ectocervical surface scraping, 1977 - 1995 (1610 patients)

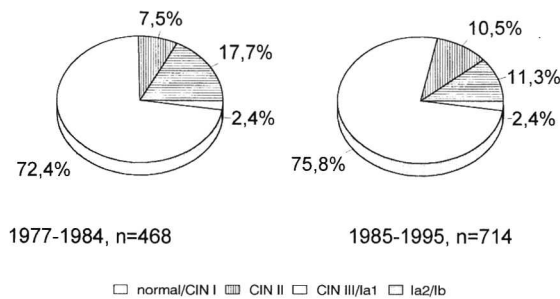


Figure 2. PAP III/IV and histological findings post conisation, 1977 - 1995 (1182 patients)

Between 1985 and 1995, 250 conisations and 328 PA at Pap III or IIID were performed. In 24.4% of the conisations and 52.4% of the PA the finding was < CIN II, whereas in 55.6% and 20.7%, respectively, the finding was CIN III/Ia1 (Fig. 3).

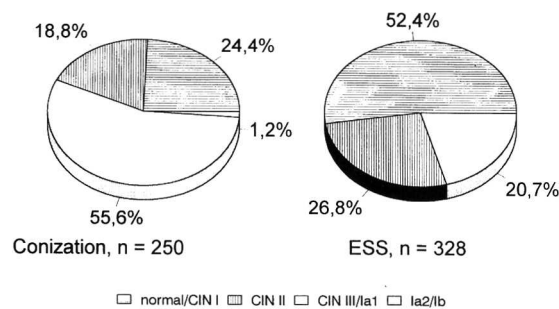


Figure 3. PAP III and histological findings post conisation or ectocervical surface scraping, 1985 - 1995 (578 patients)

Biopsy and ectocervical surface scraping for cytology of Pap III, IIID, IVa and IVb showed histological correspondence in 44.6% of the cases. At 49.5% for Pap II/IIID findings alone, this value was only insignificantly higher. In 22.3% of all cases the highest CIN degree was determined by colposcope-guided biopsy. In 33.1% of the cases the most extensive dysplasia was seen in the material obtained by ectocervical surface scraping, in 12 cases (9.2%) a major difference (CIN III) was detected (Fig. 4).

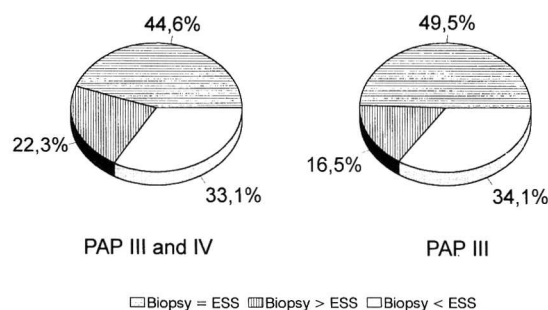


Figure 4. Comparison of histological findings post biopsy and ectocervical surface scraping at Pap III or IV (130 patients)

DISCUSSION AND CONCLUSIONS

Morphological results indicating that no atypical epithelial structures/CIN I were seen in as many as 50% of all conisation cases abound both in literature and at scientific events (7, 12, 15). Consequently, it is indispensable to step up quality assurance. With 14% of all conisations with findings < CIN II (1977-1995, at Pap III, IIID, IVa and IVb, respectively), the results for our own patients are not satisfactory, either (Abb. 1). For they represent conisations that could have been avoided and are clearly examples of over-treatment. The ideal should be to do without conisation in women of childbearing age, unless atypical structures of at least CIN II, preferably of CIN III, are detected. To be realistic, the aim should be to come as close as possible to this ideal.

Because of its high proportion of false-positive smears, the preoperative cytologic finding is unsuitable as the only criterion upon which the indication of conisation is based. The example of the Pap III/IIID cytology shows that this insecurity can hardly be overcome by repeating smears. When histological clarification became possible thanks to the advent of ectocervical surface scraping, the number of conisations with histological evidence of (CIN I was reduced by some 64%) (Fig.2). Our own cases also comprise a growing number of uncertain cell tests (Pap III/IIID) with virus-associated mild and moderate dysplasia (Fig. 5).

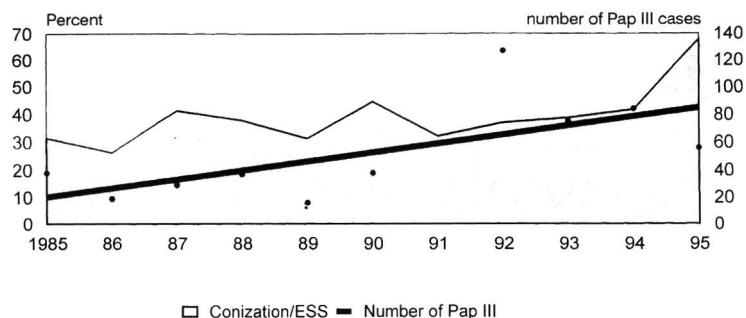


Figure 5. Percentage of histological findings without cellular atypia/CIN I post conisation or ectocervical surface scraping/cervical abrasion (233 of 578 patients) and absolute number of Pap III cases, trend analysis 1985 - 1995.

The decision to perform either superficial scraping and endocervical abrasion or conisation and cervical abrasion depended on the woman's intention to bear children, if the cytologic evidence was identical and changes were detected by colposcopy. This critical attitude to initial cytologic findings is confirmed by histological findings for the period from 1985 to 1995: In 24.4% of conisation and 52.4% of PA cases the finding was < CIN II and in 55.6% and 20.7%, respectively, CIN III/Ia1. Among conisation cases, there is clearly greater histological evidence of CIN III and Ia1 findings (Fig. 3). This statement applies both to cell tests of Pap III/IIID and, at a higher level, to Pap IVa/IVb. Cytologic findings show a good correlation with the histologically confirmed degree of CIN. Colposcopy helps to differentiate identical cytologic findings and thus clearly facilitates the decision whether a patient should be treated with conisation or simpler biopsy techniques. From our cases of the last decade (519 ectocervical surface scrapings at Pap II - IV), 250 women with max. CIN-I benefited from it, for conisation was not performed.

It is noteworthy that in both cytology groups there is a number of cases with abnormal epithelium or CIN-1 findings. These findings alone would not permit conisation. From 1985 to 1995, the share of 4% may have been acceptable for Pap IV and conisation, but not for the group with Pap III and conisation, where the percentage of 24.4% is difficult to justify (Fig. 3). That is to say that in almost one in four patients only anomalous or slightly dysplastic epithelium was detected.

In a prospective randomised comparative study, Egger et al. (3) demonstrated the greater diagnostic certainty and safety of ectocervical surface scraping and cervical abrasion in comparison with conisation and vaginal hysterectomy. This gave rise to a debate. As early as 1956 (8), Hillemanns stated that the requirements made on the histological specimen are not adequately met, especially as far as evidence of invasion is concerned. Although Egger et. al. state that the diagnostic reliability of ectocervical surface scraping and cervical abrasion as a means to determine subsequent therapy is $p < 0.01$, our results show that ectocervical surface scraping alone does not permit to establish a reliable diagnosis. After all, in 22.3% of the cases undergoing both biopsy and ectocervical surface scraping, biopsy was superior to ectocervical surface scraping, whereas in 33.1% of all cases ectocervical surface scraping was superior to biopsy (Fig. 4). In 12 cases (9.2%) the results were CIN III against (CIN II. The reasons can only be determined by analysing the colposcopic findings for PA and biopsy (PE). If the punctum maximum cannot be clearly identified by colposcope, PE alone can be expected to result in an unreliable diagnosis.

Biopsy or ectocervical surface scraping alone or combined with cervical abrasion are no adequate substitute for conisation. If colposcopy does not result in a definite ectocervical finding, these three biopsy techniques should be applied in combination.

The above results substantiate the following principle: Conisation as the only diagnostic procedure is unnecessary and can be replaced by combined simpler biopsy techniques ensuring the same level of safety. It goes without saying that conisation is a significant therapeutic method for women with CIN III lesions who intend to bear children, although techniques such as loop-excision with colposcopic and cytologic follow-up will become ever more important in this context (6).

In the presence supplementary indications in women who do not intend to bear more children and in the event of evidence of early invasion, vaginal hysterectomy should be performed instead of conisation.

The evaluation of histological findings of these excision biopsies may be used in training courses for quality assurance in colposcopy. The correspondence between pre-operative cytology and histological findings in the biopsy material depends on the training of the gynaecologist performing the colposcopy, and ideally he should also carry out the operation. The results outlined in this paper apply only to an average hospital with alternating staff and not to special dysplasia consultations which are indispensable in the light of the available results.

Suspect and pathological cytologic findings in groups III to V must be resolved by histology as soon as possible. Cytologic examination is compulsory for Pap III, but also helps to limit the percentage of false-positive findings in other pathological cytologic tests and is a contribution to quality assurance. Differential colposcopy with 3% acetic acid demonstrates HPV infection (5). If need be, virus-associated lesions are classified according to COPPLESON (2). Before a definite therapeutic decision is taken, the indication for patients intending to bear children should be verified.

The application of sparing biopsy techniques is recommended in particular for CIN diagnosis during pregnancy. In this case, ectocervical surface scraping and targeted biopsy have long been preferred to conisation (4,9).

If there is well-founded suspicion of CIN I or CIN II lesions, surface-destroying methods such as laser vaporisation or flat loop-excision are sufficient. The overwhelming majority of patients in whom biopsy and superficial destruction are performed in one session benefit from the advantages that are claimed for conisation, namely diagnosis combined with definitive therapy, without having to put up with its definite disadvantages. This demand is corroborated by findings about virus-associated epithelial lesions in younger age. Unnecessary conisation is performed in too many cases. In conisations, as in mamma biopsies and endoscopic surgery for ovarian cysts, quality assurance in the operative CIN management should also be based on an acceptable ratio of benign to atypical or malignant findings.

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Summary

Between 1977 and 1995, a total of 1610 patients were admitted to hospital with Pap III, IIID, IVa or IVb. The results of 1182 conisations with cervical abrasion and 428 ectocervical surface scrapings with cervical abrasion were evaluated. The percentage of findings of (CIN II was 35.2 % for all cases and 23.3 % for conisation alone. No atypical findings or CIN I was seen in 13.9% of all conisation cases. The introduction of a second biopsy method (ectocervical surface scraping (ESS) in 1985 resulted in the reduction of cases with a positive histological finding for conisations of (CIN I from 17.7% (1977 - 1984, n = 468) to 11.3 % (1985 - 1995, n = 714).

Evaluation of combined PA and punch biopsy from the ectocervix assisted by colposcopy was performed in 130 cases. Histological correspondence between the methods was seen in 44.6 % of the cases. In 22.3 % of the patients the highest CIN degree was seen in the biopsy material obtained under colposcopic observation, while in 33.1 % of the cases the highest degree of dysplasia was seen in the material obtained by ectocervical surface scraping.

Conisation as the sole diagnostic tool can be replaced by combined and simplified biopsy techniques without prejudice to safety. If only PA is performed, the possibility cannot be ruled out that in individual cases an early-stage invasive cervical carcinoma may be overlooked.

Conisation performed without evidence of atypical epithelial structures or only CIN I findings must be regarded as over-treatment. For all CIN III cases, however, conisation remains the most important form of therapy.

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